LINEAR BENZOCHROMANONES AND BENZOCHROMONES*

II. SYNTHESIS OF 6,7-CYCLOHEXENOCHROMANONE, 6,7-BENZOCHROMANONE, 6,7-CYCLOHEXENOCHROMONE, AND 6,7-BENZOCHROMONE

By K. H. BELL† and H. DUEWELL†

[*Manuscript received March* 22, 1963]

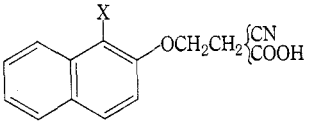
Summary

6,7-Cyclohexenochromanone, 6,7-benzochromanone, 6,7-cyclohexenochromone, and 6,7-benzochromone have been synthesized from a common starting material, 5,6,7,8-tetrahydro-2-naphthol. 6,7-Benzochroman has been obtained as a reaction by-product.

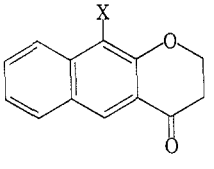
I. INTRODUCTION

In Part I of this series [1] a number of linear benzochromanones were prepared by ring closure of suitably substituted naphthalenes. The presence of blocking groups prevented the formation of angular isomers (I→II).

Electrophilic substitution of 5,6,7,8-tetrahydro-2-naphthol (IIIa), which is essentially a 3,4-dialkylphenol, usually takes place in the 3-position with the formation of the symmetrical isomer. This is shown, for example, by the Fries rearrangement of 5,6,7,8-tetrahydro-2-naphthylacetate to yield 5,6,7,8-tetrahydro-2-hydroxy-3-acetonaphthone (IIIb)[2] and nitration of (IIIa) to yield the 3-nitro derivative.[3] Thus it was thought that application of the reactions used in Part I of this series (I→II) to (IIIa) would yield the linear 6,7-cyclohexenochromanone (IV), from which the unsubstituted 6,7-benzochromanone (V) could be obtained by dehydrogenation.



(I)



(II)

II. RESULTS AND DISCUSSION

Reaction of acrylonitrile with (IIIa) in the presence of "Triton B" (trimethylbenzylammonium hydroxide)[4] gave 3-(5,6,7,8-tetrahydro-2-naphthyloxy) propionitrile (IIIc) which, on hydrolysis with dilute hydrochloric acid gave the corresponding acid (IIId) in an overall yield of 50%. Formation of the above acid by direct reaction of

* The paper by Bell and Duewell[1] is regarded as Part I of this series.

† Department of Chemistry, Newcastle University College, The University of New South Wales, Tighe's Hill, N.S.W.

[1] Bell, K. H., and Duewell, H. (1963).—*Aust. J. Chem.* **16**: 101.

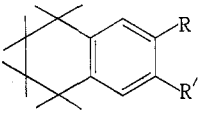
[2] O'Farrell, M. P., Wheeler, D. M. S., Wheeler, M. M., and Wheeler, T. S. (1955).—*J. Chem. Soc.* **1955**: 3986.

[3] Woodcock, D., and Clifford, D. R. (1957).—*J. Chem. Soc.* **1957**: 4139.

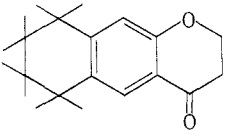
[4] Bachmann, G. B., and Levine, H. A. (1947).—*J. Amer. Chem. Soc.* **69**: 2341.

the naphthol (IIIa) with 3-bromopropionic acid was not feasible because of the insolubility of the naphthol in the strongly alkaline medium necessary for the reaction.

Cyclization of the acid (IIId) to 6,7-cyclohexenochromanone (IV) was effected smoothly and in good yield with polyphosphoric acid.



(IIIa; R = OH, R′ = H)
(IIIb; R = OH, R′ = $COCH_3$)
(IIIc; R = $O(CH_2)_2CN$, R′ = H
(IIId; R = $O(CH_2)_2COOH$, R′ = H
(IIIe; R = OH, R′ = $COCH_2CHO$



(IV)

Catalytic dehydrogenation of the above chromanone (IV) with palladium–charcoal under conditions similar to those employed by O'Farrell *et al.*[2] for the dehydrogenation of 5,6,7,8-tetrahydro-2-hydroxy-3-acetonaphthone (IIIb) to 2-hydroxy-3-acetonaphthone (VIa) yielded a mixture of two main products. One was the expected pale yellow 6,7-benzochromanone (V) obtained in low yield only. The major product was colourless, showed no carbonyl absorption in the infrared, and its ultraviolet spectrum closely resembled that of nerolin (2-naphthyl methyl ether). Newman and Zahm[5] have shown that catalytic dehydrogenation of 5,6,7,8-tetrahydro-2-acetonaphthone results in considerable reduction of the keto group and 2-ethylnaphthalene is the main product of the reaction. Thus on the basis of the above evidence and analytical data, the colourless compound was formulated as 6,7-benzochroman (VII). This assignment was supported by an examination of the n.m.r. spectrum which showed triplets at $\tau = 5{\cdot}78$ and $7{\cdot}05$ (O–$\underline{CH_2}$ and Ar–$\underline{CH_2}$ respectively) and a quintet at $\tau = 8{\cdot}0$ (CH_2–$\underline{CH_2}$–CH_2).

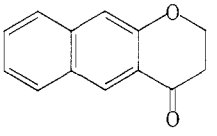
In an attempt to avoid reduction the dehydrogenation was carried out using the classical method of heating with sulphur. 6,7-Benzochromanone (V) was obtained in low yield and accompanied by considerable amounts of dark reaction by-products.

One convenient synthesis of chromones involves the Claisen condensation of ethyl formate with *o*-hydroxyaryl alkyl ketones followed by acid cyclization of the resulting keto-aldehyde. This method has been used for the synthesis of chromone itself,[6] 5,6-benzochromone,[7] and 7,8-benzochromone.[8]

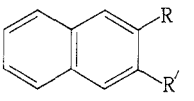
Condensation of ethyl formate with 5,6,7,8-tetrahydro-2-hydroxy-3-acetonaphthone (IIIb), obtained as indicated previously, in the presence of sodium, gave the keto-aldehyde (IIIe), which was readily cyclized to 6,7-cyclohexenochromone (VIII) with ethanolic sulphuric acid. The ultraviolet spectrum of this substance conformed to the general ultraviolet spectral pattern of chromones observed by Ganguly and Bagchi.[9] Similarly, 2-hydroxy-3-acetonaphthone (VIa), obtained by catalytic

[5] Newman, M. S., and Zahm, H. V. (1943).—*J. Amer. Chem. Soc.* **65**: 1097.
[6] Schönberg, A., and Sina, A. (1950).—*J. Amer. Chem. Soc.* **72**: 3396.
[7] Menon, B. K., and Venkataraman, K. (1931).—*J. Chem. Soc.* **1931**: 2591.
[8] Pfeiffer, P., and Grimmer, J. (1917).—*Ber. dtsch. chem. Ges.* **50**: 911.
[9] Ganguly, B. K., and Bagchi, P. (1956).—*J. Org. Chem.* **21**: 1415.

dehydrogenation of the tetrahydro derivative (IIIb) as outlined above, yielded the keto-aldehyde (VIb) which was similarly cyclized to 6,7-benzochromone (IX).

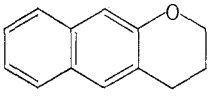


(V)

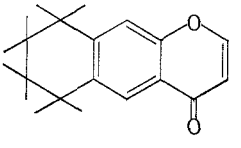


(VIa; R = OH, R′ = $COCH_3$)
(VIb; R = OH, R′ = $COCH_2CHO$)

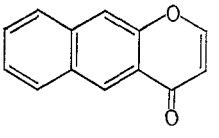
Hydrogenation of 6,7-cyclohexenochromone (VIII) in the presence of Adams' catalyst yielded the corresponding chromanone (IV), isolated separately as the 2,4-dinitrophenylhydrazone and oxime. Similarly, reduction of 6,7-benzochromone (IX)



(VII)



(VIII)



(IX)

yielded (V), isolated as the 2,4-dinitrophenylhydrazone. The calculated amount of hydrogen for reduction of the olefinic linkage only was used, as chromanones readily undergo further hydrogenation to chromans.[10] This reaction confirms the structures of the chromanones (IV) and (V).

III. Experimental

Melting points are corrected. Microanalyses are by the C.S.I.R.O. and University of Melbourne Microanalytical Laboratory. Ultraviolet spectra were measured with a Unicam SP 500 instrument and infrared spectra with a Perkin–Elmer 237 instrument. The n.m.r. spectrum was measured with a Varian DP60 instrument at 60 Mc/s on a saturated solution in deuterochloroform using tetramethylsilane as internal standard. Light petroleum refers to the fraction of b.p. 60–80°C.

(*a*) *5,6,7,8-Tetrahydro-2-naphthol.*—The method used was similar to that described by Stork.[11]

2-Naphthol (72 g) in ethanol (total volume 250 ml) and glacial acetic acid (1 ml) was hydrogenated in a rocking autoclave at 150–160°C using Raney nickel catalyst (approx. 2 g of W4).[12] The initial pressure was 120 atm and the reaction was complete within 25–30 min. The catalyst was filtered off, the solvent removed *in vacuo*, and the oily residue taken up in ether (250 ml). Extraction with 2% NaOH (5 × 400 ml) followed by acidification of the alkaline extracts yielded a pale yellow oil, which was taken into ether, the ethereal soln. dried ($MgSO_4$), and the solvent removed. Distillation of the residue gave 5,6,7,8-tetrahydro-2-naphthol (36 g, 49%), b.p. 133–134°C/3 mm, which crystallized from light petroleum as colourless plates, m.p. 59–60°C (lit. 59–60°C).

(*b*) *3-(5,6,7,8-Tetrahydro-2-naphthyloxy)propionitrile.*—5,6,7,8-Tetrahydro-2-naphthol (14·8 g; 0·1 mole), acrylonitrile (27 ml; 0·4 mole), and 40% Triton B (1 ml) were refluxed on a boiling water-bath for 24 hr. The cooled soln. was poured into cold 2% NaOH (500 ml) and the insoluble oil taken into ether. The ethereal soln. was washed with 2% NaOH, water, dried ($MgSO_4$), and the solvent removed. Distillation of the residue gave *3-(5,6,7,8-tetrahydro-2-naphthyloxy)propionitrile* (12 g, 60%), b.p. 173–175°C/2 mm, which crystallized from light petroleum as colourless

[10] Campbell, N. (1959).—"Chemistry of Carbon Compounds" (Ed. E. H. Rodd.) Vol. IVB. p. 896. (Elsevier: Amsterdam.)

[11] Stork, G. (1947).—*J. Amer. Chem. Soc.* **69**: 576.

[12] Linstead, R. P., Elvidge, J. A., and Whalley, M. (1955).—"Modern Techniques of Organic Chemistry." pp. 91, 84. (Butterworths: London.)

needles, m.p. 45°C (Found: C, 77·7; H, 7·4; N, 7·2%. Calc. for $C_{13}H_{15}NO$: C, 77·6; H, 7·5; N, 7·0%).

(*c*)*3-(5,6,7,8-Tetrahydro-2-naphthyloxy)propionic Acid.*—The above nitrile (20 g), conc. HCl (1200 ml), and water (600 ml) were refluxed for 24 hr. As the hydrolysis proceeded the oily droplets of nitrile were replaced by colourless needles of the acid. The mixture was cooled in ice, the precipitated acid filtered off, washed with water, and dried. Recrystallization from light petroleum gave colourless needles of *3-(5,6,7,8-tetrahydro-2-naphthyloxy)propionic acid* (18·1 g, 83%), m.p. 157·5–158°C (Found: C, 70·5; H, 7·3%. Calc. for $C_{13}H_{16}O_3$: C, 70·9; H, 7·3%).

(*d*) *6,7-Cyclohexenochromanone.*—The polyphosphoric acid was prepared by heating P_2O_5 (200 g) and 85% H_3PO_4(150 ml) at 130–140°C until solution was complete (2–3 hr).

The above acid (10 g) was added to the polyphosphoric acid and the mixture heated at 100–105°C for 1 hr with occasional shaking. The orange-red mixture was cooled, poured into ice-water, and the liberated gum taken up in benzene. The benzene soln. was washed, dried ($MgSO_4$), the solvent removed, and the residue fractionated *in vacuo*. *6,7-Cyclohexenochromanone* was obtained as a very pale yellow oil (6·2 g, 67%), b.p. 155–156°C/2 mm(Found: C, 77·3; H, 7·0%. Calc. for $C_{13}H_{14}O_2$: C, 77·2; H, 7·0%). Soln. in conc. H_2SO_4 is bright yellow.

2,4-Dinitrophenylhydrazone, red crystals from chloroform–methanol, m.p. 269–270°C (decomp.)(Found: N, 14·2%. Calc. for $C_{19}H_{18}O_5N_4$:N, 14·7%); u.v. spectrum (chloroform): $\lambda_{max.}$ 398 mμ (log ϵ 4·46).

Oxime, colourless needles from light petroleum, m.p. 122·5–123°C(Found: C, 72·1; H, 7·1; N, 6·5%. Calc. for $C_{13}H_{15}O_2N$: C, 71·8; H, 7·0; N, 6·5%).

(*e*)*Dehydrogenation of 6,7-Cyclohexenochromanone.*—(i)*Catalytic Dehydrogenation.* 6,7-Cyclohexenochromanone (2 g) and 30% Pd–C (0·2 g)[5] were heated under a stream of CO_2 in a metal-bath maintained at 230–240°C for 1 hr. The cooled product was taken up in ether, filtered from catalyst, the solvent removed, and the brown oil remaining chromatographed over alumina (200 g). Elution with light petroleum gave a colourless eluate with a blue fluorescence which yielded a colourless solid on evaporation. Recrystallization from methanol gave colourless needles of *6,7-benzochroman* (0·8 g), m.p. 110–111°C (Found: C, 85·0; H, 6·6%. Calc. for $C_{13}H_{12}O$: C, 84·7; H, 6·6%); u.v. spectrum (cyclohexane): $\lambda_{max.}$ 236, 262, 272, 282, 294, 321, 337 mμ(log ϵ 4·88, 3·50, 3·65, 3·73, 3·59, 3·40, 3·56); cf. 2-naphthyl methyl ether: $\lambda_{max.}$ 228, 262, 272, 282, 301, 314, 329 mμ (log ϵ 4·84, 3·63, 3·67, 3·50, 2·93, 3·23, 3·32).

Elution with benzene–light petroleum (1:1) gave a yellow oil which slowly crystallized. Recrystallization from aq. methanol gave pale yellow needles of *6,7-benzochromanone* (0·25 g), m.p. 131–132°C(Found: C, 79·1; H, 5·0%. Calc. for $C_{13}H_{10}O_2$: C, 78·8; H, 5·1%). Soln. in conc. H_2SO_4 is bright yellow.

2,4-Dinitrophenylhydrazone, red crystals from chloroform–methanol, m.p. 252–254°C (decomp.) (Found: C, 60·3; H, 4·0; N, 14·7%. Calc. for $C_{19}H_{14}O_5N_4$: C, 60·3; H, 3·7; N, 14·8%); u.v. spectrum(chloroform): $\lambda_{max.}$ 397 mμ (log ϵ 4·48).

(ii) *Sulphur Dehydrogenation.* 6,7-Cyclohexenochromanone (1·2 g) and powdered sulphur (0·38 g; theoretical) were heated in a stream of CO_2 in a metal-bath. H_2S was evolved at 180°C and the temp. was slowly raised to 250°C and held there until no further evolution of gas took place (10 min). The crude product was worked up as before. Elution with benzene–light petroleum (1:1) gave 6,7-benzochromanone (0·28 g; 24%), m.p. 130–131°C, after crystallization from aq. methanol. A large number of coloured bands were apparent on the alumina column.

(*f*) *5,6,7,8-Tetrahydro-2-naphthylacetate.*—Crushed ice (300 g) was added to a soln. of 5,6,7,8-tetrahydro-2-naphthol (30 g) in 2% NaOH (750 ml) followed by acetic anhydride (45 ml). The mixture was shaken vigorously for 20 min and the insoluble oil taken into carbon tetrachloride. The organic extract was washed with 1N Na_2CO_3, then water, dried ($MgSO_4$), and the solvent removed. Distillation of the residue gave 5,6,7,8-tetrahydro-2-naphthylacetate (30 g, 78%), colourless oil, b.p. 137–138°C/3 mm. Schroeter *et al.*[13] give b.p. 158°C/14 mm.

[13] Schroeter, G., Svanoe, H., Einbeck, H., Geller, H., and Riebensahm, E. (1922).—*Liebigs Ann.* **426**: 83.

(*g*) *5,6,7,8-Tetrahydro-2-hydroxy-3-acetonaphthone.*—Prepared according to O'Farrell *et al.*[2] from the above acetate and obtained as pale yellow needles from methanol, m.p. 71–72°C(report 72–73°C), yield 48%.

(*h*) *5,6,7,8-Tetrahydro-2-hydroxy-3-naphthoylacetaldehyde.*—A soln. of 5,6,7,8-tetrahydro-2-hydroxy-3-acetonaphthone (5 g) and ethyl formate (10 ml; dried over K_2CO_3 and freshly distilled) in anhyd. ether (25 ml) was added with shaking and cooling to a suspension of powdered Na(2 g) in anhyd. ether (25 ml). A reaction soon set in and after allowing the mixture to stand at room temp. for 24 hr the resulting yellow mass was carefully decomposed with ice-water. The aq. soln. was separated from the ether layer, extracted with a fresh portion of ether, and acidified with dil. H_2SO_4. The initial oil soon solidified to a yellow solid which was filtered off, washed with water, and dried. Recrystallization from benzene (charcoal) gave *5,6,7,8-tetrahydro-2-hydroxy-3-naphthoylacetaldehyde* (4·1 g, 72%), colourless plates, m.p. 130–131°C, which gave a reddish brown colour with alc. $FeCl_3$ (Found: C, 71·3; H, 6·4%. Calc. for $C_{13}H_{14}O_3$: C, 71·5; H, 6·5%).

(*i*) *6,7-Cyclohexenochromone.*—The above keto-aldehyde (1 g) was refluxed with ethanol (25 ml) and conc. H_2SO_4(5 ml) on a boiling water-bath for 1 hr. The cooled soln. was poured into ice-water, the ppt. filtered off, washed with water, and dried. Recrystallization from aq. ethanol gave colourless needles of *6,7-cyclohexenochromone* (0·8 g, 87%), m.p. 123°C (Found: C, 78,2; H, 6·1%. Calc. for $C_{13}H_{12}O_2$: C, 78·0; H, 6·1%). Yellow soln. in conc. H_2SO_4 has blue fluorescence; u.v. spectrum (ethanol): $\lambda_{max.}$ 224, 244, 249·5, 268, 308–309 mμ (log ε 4·38, 4·15, 4·13, 3·87, 3·89), $\lambda_{min.}$ 238, 248, 264, 287–288 mμ (log ε 4·11, 4·12, 3·86, 3·61).

Oxime, colourless needles from benzene, m.p. 166–167°C(Found: C, 72·2; H, 6·2; N, 7·0%, Calc. for $C_{13}H_{13}O_2N$: C, 72·5; H, 6·1; N, 6·5%).

(*j*) *2-Hydroxy-3-acetonaphthone.*—Prepared by dehydrogenation of 5,6,7,8-tetrahydro-2-hydroxy-3-acetonaphthone according to O'Farrell *et al.*[2] and obtained as yellow plates from light petroleum, m.p. 112–113°C (reported 111–113°C), yield 46%.

(*k*) *2-Hydroxy-3-naphthoylacetaldehyde.*—Prepared similarly to the tetrahydro compound from 2-hydroxy-3-acetonaphthone. Recrystallization from benzene gave pale yellow needles of *2-hydroxy-3-naphthoylacetaldehyde* (70%), m.p. 238–240°C(decomp.), which gave a reddish brown alc. $FeCl_3$ colour(Found: C, 73·1; H, 4·9%. Calc. for $C_{13}H_{10}O_3$: C, 72·9; H, 4·7%).

(*l*) *6,7-Benzochromone.*—Cyclization of the above keto-aldehyde was carried out essentially as described for the tetrahydro compound. Recrystallization from aq. ethanol gave pale yellow needles of *6,7-benzochromone* (84%),m.p.137–138°C (Found: C, 79·4; H, 4·2. Calc. for $C_{13}H_8O_2$: C, 79·6; H, 4·1%). Soln. in ethanol has blue-violet fluorescence and yellow soln. in conc. H_2SO_4 has blue fluorescence; u.v. spectrum (ethanol): $\lambda_{max.}$ 246, 267 (shoulder only), 276, 292–294, 304–305, 318 mμ (log ε 4·82, 4·40, 4·32, 3·99, 4·02, 3·97), $\lambda_{min.}$ 227, 274, 288, 296, 314–315 mμ (log ε 4·53, 4·31, 3·98, 3·98, 3·96).

Oxime, very pale yellow needles from aq. ethanol, m.p. 189–191°C(decomp.)(Found: C, 73·6; H, 4·3; N, 6·2%. Calc. for $C_{13}H_9O_2N$: C, 73·9; H, 4·3; N, 6·6%).

(*m*) *Reduction of 6,7-Cyclohexenochromone.*—6,7-Cyclohexenochromone (20 mg) in glacial acetic acid (1 ml) was shaken with Adams' catalyst[12] (2·8 mg) under hydrogen at room temp. and pressure in a microhydrogenation apparatus until the theoretical volume of hydrogen was absorbed (2·44 ml at 24°C and 760 mm). The catalyst was filtered off and the solvent removed *in vacuo*. The remaining oil was converted directly to the DNP derivative, m.p. 268–269°C (decomp.), identical with the DNP of 6,7-cyclohexenochromanone. In another reduction the oil was converted directly to the oxime, m.p. 122–123°C, identical with the oxime of 6,7-cyclohexenochromanone.

(*n*) *Reduction of 6,7-Benzochromone.*—Carried out similarly to reduction of 6,7-cyclohexenochromanone. The product was converted directly to the DNP derivative, m.p. 252–254°C (decomp.), identical with the DNP of 6,7-benzochromanone.

IV. Acknowledgment

The authors wish to thank Dr. T. J. Batterham, United States National Institutes of Health, Bethesda, U.S.A., for the measurement of the n.m.r. spectrum.